Tetrahedron. Vol. 24, pp. 6453 to 6457. Pergamon Press 1968. Printed in Great Britain

CHEMICAL CONSTITUTION AND ACTIVITY OF BIPYRIDYLIUM HERBICIDES—III*

PYRAZINO[1.2.3.4-*lmn*]1,10-PHENANTHROLINIUM DIBROMIDE

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(*Received in the UK* 4 *June* 1968; *accepted for publication* 26 *June* 1968)

Abstract—The synthesis of 5,6-dihydro-5-hydroxy-pyrazino[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide and the new aromatic system pyrazino[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide from 1,10-phenanthroline is described. Both salts are reduced in aqueous solution by a one electron transfer to give relatively unstable radical cations. In accord with current theory on the mode of action of bipyridylium herbicides they are essentially inactive as herbicides.

THE mode of action of the bipyridylium herbicide diquat (I) is thought[1–4] to be connected with its ability to be rapidly reduced in aqueous solution by a one electron transfer at a potential (E_0) of about $-0{\cdot}35$ volts to give a stable radical cation II which is rapidly and quantitatively reversed by oxygen. Certain bridged diquaternary salts of 1,10-phenanthroline (e.g. III and X) behave similarly on reduction although they are less active as herbicides.[5–7] The reasons for the lower level of activity may be due to the higher reduction potential of the phenanthroline salts ($\sim -0{\cdot}27$ volts) and to the fact that the one electron transfer is not quite quantitatively reversed by air. The related tricyclic aromatic system, dipyrido[1.2-*a*:2′.1′-*c*]pyrazinium dibromide (IV) has properties of one electron transfer like the phenanthroline salts and shows appreciable phytotoxicity although it too is not as active a herbicide as diquat.[8] This paper describes the preparation and some of the properties of the corresponding tetracyclic aromatic system, pyrazino-[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide (V). Parts of the work have been reported in a preliminary communication.[9]

The synthesis of V was accomplished from 1,10-phenanthroline by modifying methods recently developed by groups in Australia[10] and Britain[11] for the synthesis of IV from 2,2′-bipyridyl. 1,10-Phenanthroline was converted to the quaternary salt VI by reaction with bromoacetaldehyde 2,4-dinitrophenylhydrazone in benzene solution. The salt VI was cyclized by concentrated aqueous hydrobromic acid to 5,6-dihydro-5-hydroxypyrazino[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide (VII), the structure of which was confirmed by elemental analyses (all bromine ionic) and by the NMR spectrum. Compound VII was dehydrated with thionyl chloride to the fully aromatic tetracyclic system V which was obtained crystalline from a mixture of acetone and aqueous hydrobromic acid. The structure V was consistent with elemental analyses (all bromine ionic) and with the NMR spectrum in D_2O, the protons in positions 5 and 6 being clearly discerned as a singlet at $\delta = 9{\cdot}4$ ppm.

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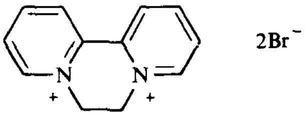
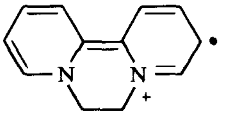
* Part II, L. A. Summers, *Tetrahedron* **24**, 5433 (1968).



I



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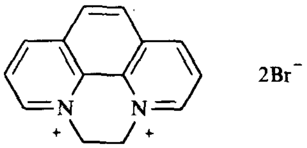

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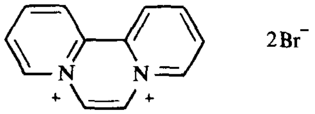
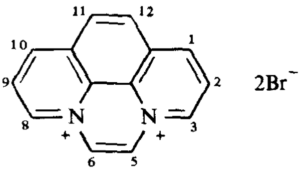
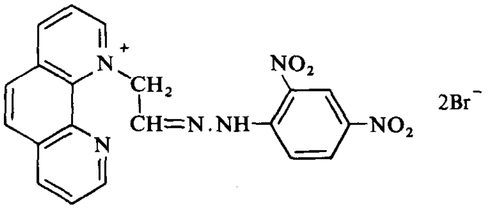


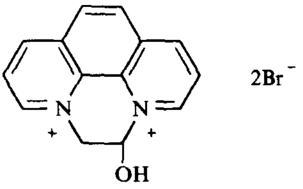
IV



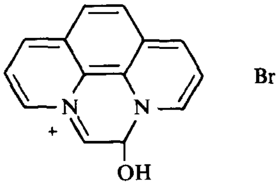
V



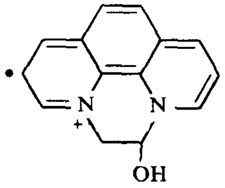
VI



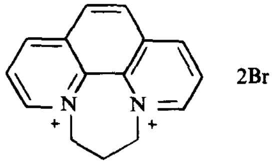
VII



VIII



IX



X

The diquaternary salts VII and V are reactive compounds and are much less easily handled than the corresponding compounds[8,10,11] prepared from 2,2′-bipyridyl; they are difficult to purify and readily deteriorate in hot hydroxylic solvents to give highly colored solutions. When pure, VII and V are stable in aqueous solution. Compound V is in reversible equilibrium dependent on pH, with another species which is deep red in colour and is considered to be the pseudo base VIII (Fig. 1). The red form predominates at pH values above about 6·8. Both VII and V are decomposed by strong alkali.

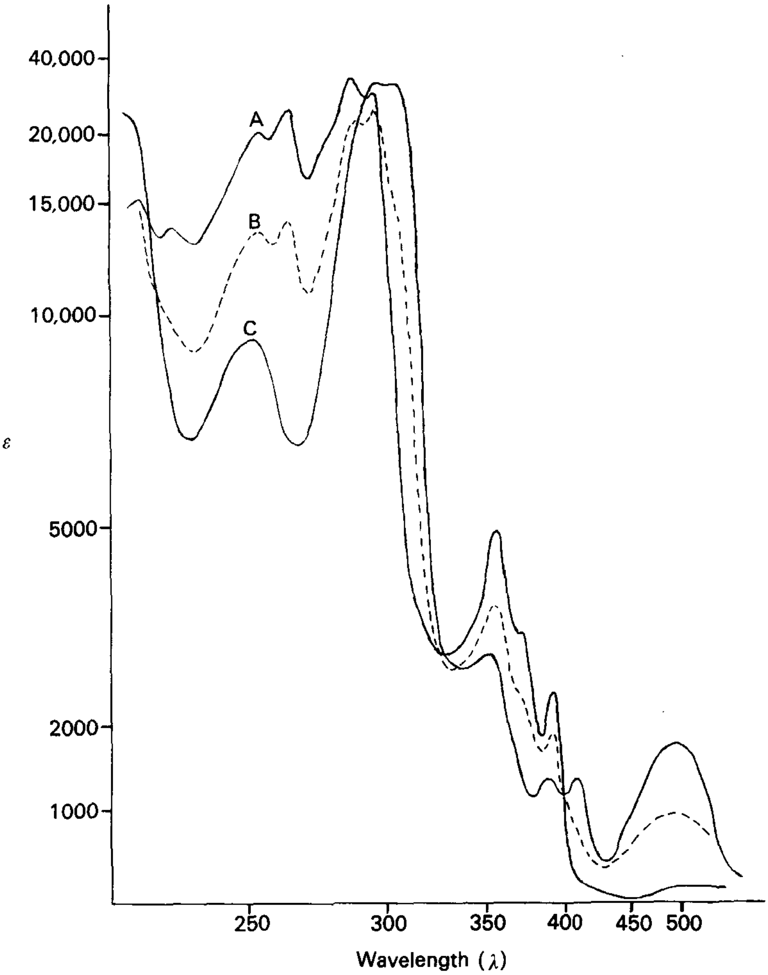


FIG. 1 UV spectrum of Pyrazino[1.2.3.4-*lmn*]1,10-phenanthrolinium dibromide. A, pH 4·6; B, pH 5·9; C, pH 8·0.

An aqueous solution of VII on treatment with zinc dust immediately developed a brown-red coloration which is attributed, at least in part, to the radical cation of which IX is one canonical form. The presence of a paramagnetic species in the colored solution was confirmed by the observation that it gave a degenerate and poorly resolved NMR spectrum. The appearance of a few signals which are absent in the spectrum of VII is attributed to products obtained by the decay of IX. This suggests that the radical cation IX is less stable than the radical cations derived from the unhydroxylated diquaternary salts III and X[7]. When the reducing agent was removed and the solution was shaken in air for 15 min a complex mixture of products was obtained (NMR evidence). Results obtained from polarography were consistent with the uptake of one electron by VII. At concentrations of 0·001M and 0·0015M in the pH range 3·3–7·4 it gave a typical symmetrical one electron reduction wave with a half-wave potential (E_0) of −0·18 V independent of pH and concentration.

It is evident from these results that the diquaternary salt VII is reduced by a one electron transfer in aqueous solution to give a radical cation but unlike the diquaternary salts III and X[7] the one electron transfer is not substantially reversed by air.

An aqueous solution of V on treatment with zinc dust immediately developed an intense violet coloration. The NMR spectrum of the violet solution taken 30 min after the addition of the zinc showed no evidence of the presence of a high concentration of a stable free radical species[5,6,8] but indicated that about 50% of V had been converted to a complex mixture of reaction products. On polarographic examination in the pH range 3·3–5·0 at concentrations of 0·001M and 0·0005M, V gave an almost symmetrical reduction wave which approximated to the uptake of one electron with a half-wave potential (E_0) of about $-0{\cdot}12$ V independent of pH and concentration. At higher pH values the wave height decreased in size and disappeared above pH 6·8. Simultaneously a reduction wave appeared at a much lower potential ($\sim -0{\cdot}80$ V) attributed to the reduction of the pseudo base VIII. This evidence is consistent with the view that V is reduced in aqueous solution by a one electron transfer to give a rather unstable redical cation which rapidly decays to unidentified reaction products. The instability of the radical cation from V contrasts with the substantial stability[8] of the radical cation derived from the tricyclic salt IV and presumably reflects the greater reactivity of the tetracyclic system V.

In post-emergent herbicidal tests on six plant species at a rate equivalent to 8 lb/acre, the diquaternary salts V and VII showed no significant activity. These results are consistent with the theory[1–4] that for herbicidal activity of the type associated with bipyridylium salts the compounds, *inter alia* must be capable of being reduced at appropriate potentials to radical cations which are stable in aqueous solution and which are reversibly oxidized by air.

EXPERIMENTAL

Buffer solns were Britton and Robinson buffers of pH 3·3, 4·6, 5·0, 8·7 and 9·6 and Sorensen buffers of pH 5·9, 6·8, 7·4 and 8·0. UV absorption spectra were taken with 0·0001M or 0·00005M solns. Extinction coefficients and wavelengths reported previously[9] were approximate. NMR spectra were taken in D_2O at 60 Mc/s using sodium 3-trimethylsilyl-1-propane sulphonate as internal standard. Polarograph experiments were carried out on aqueous buffer solutions at 20° using a standard calomel electrode. Half-wave potentials are assumed to be E_0 values and were calculated by adding 0·25 volts to the $E_{\frac{1}{2}}$ values. Experimental error is $\pm 0{\cdot}02$ V. Microanalyses were by the Australian Microanalytical Service.

1-(β-2,4-*Dinitrophenylhydrazono*)*ethyl*-1,10-*phenanthrolinium bromide* (VI) was prepared by reacting equimolar portions of 1,10-phenanthroline hydrate and bromoacetaldehyde 2,4-dinitrophenyl-hydrazone[12] in benzene soln at 60° for 1 hr with vigorous agitation. The yellow salt, m.p. 196–200° (with dec), yield = 92%, which precipitated was collected after 3 days and was used in the next stage of the synthesis without further purification. It was difficult to crystallize but an analytical sample of the monohydrate was obtained from aqueous MeOH as yellow crystals, m.p. 205–208° (with dec). (Found: C, 47·95; H, 3·4; N, 17·0; Br, 16·6. $C_{20}H_{15}BrN_6O_4 \cdot H_2O$ requires: C, 47·9; H, 3·4; N, 16·8; Br, 16·0%).

5,6-*Dihydro*-5-*hydroxypyrazino*[1,2,3,4-*lmn*]1,10-*phenanthrolinium dibromide* (VII) was prepared by warming the salt VI (10 g) with conc HBr aq (50 ml) on a steam bath for 40 min. The dark mixture was filtered and the cold filtrate was diluted with acetone to give a ppt of the product which crystallized from aqueous acetone (charcoal) as brown crystals, m.p. > 360°, yield 70%. UV spectrum (H_2O) λ_{max} 224 (log ε 4·36), 280 (4·48), 311 (3·85), 324 mμ (3·71); NMR spectrum δ 5·75–5·85 (2H, d, methylene), 7·15–7·3 (1H, t, C$\underline{H}$—OH), 8·6–8·9 (2H, m, 2, 9 aromatic), 8·8 (2H, s, 11, 12 aromatic), 9·6–10·0 ppm (4H, m, 1, 3, 8, 10 aromatic). Reduction potential $E_0 - 0{\cdot}18$ V. (Found: C, 43·2; H, 3·45; N, 7·3; Br (ionic) 41·6. $C_{14}H_{12}Br_2N_2O$ requires: C, 43·75; H, 3·1; N, 7·3; Br (ionic) 41·7%).

Pyrazino[1.2.3.4-*lmn*]1,10-*phenanthrolinium dibromide* (V) was prepared by heating VII (7·4 g) with $SOCl_2$ (37 ml) under reflux for 1 hr. The $SOCl_2$ was removed *in vacuo* and the solid residue was treated with acetone (25 ml). The ppt which remained was crystallized from a mixture of acetone and HBr aq to give the product as buff crystals, m.p. >360°, yield = 45%; UV spectrum (H_2O, pH 4·6) λ_{max} 225 (log ε 4·18), 232 (4·13), 256 (4·30), 265 (4·36), 287 (4·46), 296 (4·41), 353 (3·70), 369 (3·52), 388 mμ (3·40) see also Fig. 1; NMR spectrum δ 8·9–9·15 (2H, m, 2,9 aromatic), 9·0 (2H, s, 11,12 aromatic), 9·4 (2H, s, 5,6 aromatic), 9·8–9·9 (2H, d, 1,10 aromatic) 10·1–10·2 ppm (2H, d, 3,8 aromatic). Reduction potential E_0 − 0·12 V. (Found: C, 45·6; H, 3·0; N, 7·9; Br (ionic) 43·7. $C_{14}H_{10}Br_2N_2$ requires: C, 45·9; H, 2·7; N, 7·65; Br (ionic) 43·7%).

Acknowledgements—The herbicide tests were kindly arranged by Dr. G. F. Katekar of the Division of Plant Industry, C.S.I.R.O., Canberra. We warmly thank Mr. V. A. Pickles of the University of New South Wales for the nuclear magnetic resonance spectra.

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